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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,515	05/01/2002	Dan L. Eaton	10466/300	8122

7590 09/08/2004

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EXAMINER	
ROMEO, DAVID S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 09/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,515	EATON ET AL.	
	Examiner	Art Unit	
	David S Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09/10/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The preliminary amendment filed 09/09/2002 has been entered. Claims 1-6 are pending and being examined.

Priority

The present application is claiming priority under 35 U.S.C. 120 and 119 (e) to earlier filed applications. Under 35 U.S.C. 120, the claims in a U.S. application are entitled to the benefit of the filing date of an earlier filed U.S. application if the subject matter of the claim is disclosed in the manner provided by 35 U.S.C. 112, first paragraph in the earlier filed application. Under 35 U.S.C. 119 (e), the claims in a U.S. application are entitled to the benefit of a foreign priority date or the filing date of a provisional application if the corresponding foreign application or provisional application supports the claims in the manner required by 35 U.S.C. 112, first paragraph. A deficiency under 35 U.S.C. 101 also creates a deficiency under 35 U.S.C. 112, first paragraph.

The presently claimed invention lacks utility for the reasons set forth in the rejections below. Hence, neither the present application nor any of the other earlier filed applications provide a disclosure in the manner provided by 35 U.S.C. 112, first paragraph. Accordingly, the effective filing date of the presently claimed compounds is 05/01/2002, which is the filing date of the present application.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are directed to or encompass an antibody that binds the polypeptide shown in SEQ ID NO: 10. The present application characterizes the PRO874 polypeptide (SEQ ID NO: 10) and polynucleotide as follows:

> [0036] FIG. 9 shows a nucleotide sequence (SEQ ID NO: 9) of a native sequence PRO874 cDNA, wherein SEQ ID NO: 9 is a clone designated herein as "DNA40621-1440".
>
> [0037] FIG. 10 shows the amino acid sequence (SEQ ID NO: 10) derived from the coding sequence of SEQ ID NO: 9 shown in FIG. 9. Page 11.
>
> DNA40621-1440 is more highly expressed in normal lung than as compared to lung tumor. Example 18, Page 141.

Figure 10 also provides various structural features of the PRO874 polypeptide, presumably based on homology with domains of other known proteins. It is noted that PRO874

is less than a full length polypeptide because the amino acid sequence of SEQ ID NO: 10 does not begin with an initiator methionine. No further characterization is provided.

The tumor versus normal differential tissue expression distribution (Example 18) provides only a use for a limited number of nucleic acid probes. No information is provided in the differential tissue expression distribution data regarding the level of expression, activity, or role in cancer of the PRO874 polypeptide. Further, differential tissue nucleic acid expression is not always correlated with protein levels. For example, Allman (U) discloses that germinal center B cells express dramatically more BCL-6 protein than resting B cells, despite similar BCL-6 mRNA levels in the two cell populations. Page 5257, paragraph bridging left and right columns. mRNA translation is regulated in many genes and can be mediated by binding of proteins to cis-acting RNA motifs in the untranslated regions of the mRNAs (paragraph bridging pages 5266-5267).

Furthermore, one skilled in the art recognizes that although structural similarity can serve to classify a protein as related to other known proteins this classification is insufficient to establish a function or biological significance for the protein because ancient duplications and rearrangements of protein-coding segments have resulted in complex gene family relationships. Duplications can be tandem or dispersed and can involve entire coding regions or modules that correspond to folded protein domains. As a result, gene products may acquire new specificities, altered recognition properties, or modified functions. Extreme proliferation of some families within an organism, perhaps at the expense of other families, may correspond to functional innovations during evolution. See Henikoff (V), page 609, Abstract. Accordingly, one skilled in the art would not accept mere homology as establishing a function of protein because gene

products may acquire new specificities, altered recognition properties, or modified functions. Rather, homology complements experimental data accumulated for the homologous protein in understanding the homologous protein's biological role. Although, the presence of a protein module in a protein of interest adds potential insight into its function and guides experiments, insight into the biological function of a protein cannot be automated. However, homology can be used to guide further research. See Henikoff (V), paragraph bridging pages 613-614, through page 614, paragraph bridging columns 1-2.

The instant claims encompass a protein of as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein identified in the specification as PRO874 one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use it. Thus, there was no immediately apparent or "real world" utility for the PRO874 polypeptide as of the filing date. After further research, a specific and substantial utility might be found for the PRO874 polypeptide of the instant invention. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The claimed antibodies lack utility because the PRO874 polypeptide, to which the claimed antibodies bind, is not supported by either a specific and substantial asserted utility or a well established utility. In the absence of either a specific and substantial asserted utility or a well established utility for the polypeptide there is no patentable utility for the antibody that binds the polypeptide.

Claims 1-6 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is indefinite over the recitation of "specifically binds." Because the instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "specifically binds" an artisan cannot determine what additional or material functional limitations are placed upon a claim by the presence of this element. The metes and bounds are not clearly set forth.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Baker (N). This rejection is based upon an effective filing date of 05/01/2002, the filing date of the present application, for the presently claimed compounds. Baker discloses an isolated polypeptide (page 55, full paragraph 4) that is identical to the amino acid sequence of SEQ ID NO: 10, as indicated below (Qy = SEQ ID NO: 10):

```
  Query Match             100.0%;  Score 1709;  DB 21;  Length 321;
  Best Local Similarity   100.0%;  Pred. No. 2.4e-181;
  Matches  321;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 RTRGRTRGGCEKVPINTSCNPTAHLVNSSCPGLMCVFQGYSSKGLIQRSVFNLQIYGVLG 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 RTRGRTRGGCEKVPINTSCNPTAHLVNSSCPGLMCVFQGYSSKGLIQRSVFNLQIYGVLG 60

Qy         61 LFWTLNWVLALGQCVLAGAFASFYWAFHKPQDIPTFPLISAFIRTLRYHTGSLAFGALIL 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 LFWTLNWVLALGQCVLAGAFASFYWAFHKPQDIPTFPLISAFIRTLRYHTGSLAFGALIL 120

Qy        121 TLVQIARVILEYIDHKLRGVQNPVARCIMCCFKCCLWCLEKFIKFLNRNAYIMIAIYGKN 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 TLVQIARVILEYIDHKLRGVQNPVARCIMCCFKCCLWCLEKFIKFLNRNAYIMIAIYGKN 180

Qy        181 FCVSAKNAFMLLMRNIVRVVVLDKVTDLLLFFGKLLVVGGVGVLSFFFFSGRIPGLGKDF 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 FCVSAKNAFMLLMRNIVRVVVLDKVTDLLLFFGKLLVVGGVGVLSFFFFSGRIPGLGKDF 240

Qy        241 KSPHLNYYWLPIMTSILGAYVIASGFFSVFGMCVDTLFLCFLEDLERNNGSLDRPYYMSK 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 KSPHLNYYWLPIMTSILGAYVIASGFFSVFGMCVDTLFLCFLEDLERNNGSLDRPYYMSK 300

Qy        301 SLLKILGKKNEAPPDNKKRKK 321
              |||||||||||||||||||||
Db        301 SLLKILGKKNEAPPDNKKRKK 321.
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Baker also discloses a chimeric polypeptide comprising the isolated polypeptide fused to heterologous polypeptide wherein the heterologous polypeptide is an epitope tag or a Fc region of an immunoglobulin (page 280, lines 32-35), and monoclonal, polyclonal, and humanized antibodies, and antibody fragments that bind the isolated polypeptide (page 280, last full paragraph; page 367, full paragraph 3; page 309, full paragraph 3; page 311, line 28, through page 313, line 6; pages 365-371).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 5, 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over TrEMBL protein sequence database accession no. Q9Y332 (W) in view of Sibson (O).

This rejection is based upon an effective filing date of 05/01/2002, the filing date of the present application, for the presently claimed compounds. TrEMBL discloses the translation of a coding sequence, which is 97.5% identical to SEQ ID NO: 10, as indicated below (Db = TrEMBL translation):

```
  Query Match             97.5%;  Score 1667;  DB 4;  Length 712;
  Best Local Similarity   100.0%;  Pred. No. 3.1e-144;
  Matches  313;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          9 GCEKVPINTSCNPTAHLVNSSCPGLMCVFQGYSSKGLIQRSVFNLQIYGVLGLFWTLNWV 68
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        400 GCEKVPINTSCNPTAHLVNSSCPGLMCVFQGYSSKGLIQRSVFNLQIYGVLGLFWTLNWV 459

Qy         69 LALGQCVLAGAFASFYWAFHKPQDIPTFPLISAFIRTLRYHTGSLAFGALILTLVQIARV 128
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        460 LALGQCVLAGAFASFYWAFHKPQDIPTFPLISAFIRTLRYHTGSLAFGALILTLVQIARV 519

Qy        129 ILEYIDHKLRGVQNPVARCIMCCFKCCLWCLEKFIKFLNRNAYIMIAIYGKNFCVSAKNA 188
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        520 ILEYIDHKLRGVQNPVARCIMCCFKCCLWCLEKFIKFLNRNAYIMIAIYGKNFCVSAKNA 579

Qy        189 FMLLMRNIVRVVVLDKVTDLLLFFGKLLVVGGVGVLSFFFFSGRIPGLGKDFKSPHLNYY 248
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        580 FMLLMRNIVRVVVLDKVTDLLLFFGKLLVVGGVGVLSFFFFSGRIPGLGKDFKSPHLNYY 639

Qy        249 WLPIMTSILGAYVIASGFFSVFGMCVDTLFLCFLEDLERNNGSLDRPYYMSKSLLKILGK 308
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        640 WLPIMTSILGAYVIASGFFSVFGMCVDTLFLCFLEDLERNNGSLDRPYYMSKSLLKILGK 699

Qy        309 KNEAPPDNKKRKK 321
              |||||||||||||
Db        700 KNEAPPDNKKRKK 712.
```

TrEMBL does not disclose antibodies that bind the polypeptide.

Sibson suggest expression of partial or full-length cDNAs for functional analysis of the encoded polypeptide (page 10, line 38, through page 11, line 15). Sibson also suggest making antibodies, including monoclonal antibodies, against the protein (page 11, full paragraph 2). The antibodies can be used for localization in situ (page 12, full paragraph 1). Sibson does not teach, in the sense that Sibson does not anticipate, expression of TrEMBL protein sequence database accession no. Q9Y332 and the making of antibodies thereto.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to express TrEMBL protein sequence database accession no. Q9Y332, isolate the encoded protein, and make antibodies, including monoclonal antibodies, thereto with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification for localization of the polypeptide in situ.

The word "label" when used in the present specification refers to a detectable compound or composition which is conjugated directly or indirectly to the antibody so as to generate a "labeled" antibody (page 43, full paragraph 1). The disclosure of in situ localization of a polypeptide with antibodies by Sibson is tantamount to the disclosure of labeled antibodies because it would be necessary to label the antibodies in order to localize the polypeptide. The invention is prima facie obvious over the prior art.

Claims 1, 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over TrEMBL protein sequence database accession no. Q9Y332 (W) in view of Sibson (O) as applied to claim 1 above and further in view of Brandon (X).

TrEMBL protein sequence database accession no. Q9Y332 (W) in view of Sibson (O) teach antibodies that bind TrEMBL protein sequence database accession no. Q9Y332, as discussed above. TrEMBL protein sequence database accession no. Q9Y332 (W) in view of Sibson (O) do not teach antibody fragments that bind TrEMBL protein sequence database accession no. Q9Y332.

Brandon teaches improved immunocytochemical staining through the use of Fab fragments of primary antibody (Abstract). Brandon does not teach Fab fragments of primary antibody that bind TrEMBL protein sequence database accession no. Q9Y332.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make antibodies that bind TrEMBL protein sequence database accession no. Q9Y332, as taught by TrEMBL protein sequence database accession no. Q9Y332 (W) in view of Sibson (O), and to modify that teaching by making Fab fragments of primary antibody, as taught by Brandon, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification in order to improve immunocytochemical staining. The invention is prima facie obvious over the prior art.

Conclusion

No claims are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571)272-0961.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

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FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (571) 273-0890.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

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DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

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DSR
SEPTEMBER 6, 2004